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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/560,378	01/22/2007	Toshiyuki Hori	58777.000018	9632

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EXAMINER	
HAYES, ROBERT CLINTON	
ART UNIT	PAPER NUMBER
1649	

MAIL DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/560,378	HORI, TOSHIYUKI	
	Examiner	Art Unit	
	Robert C. Hayes, Ph.D.	1649	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 June 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-25* is/are pending in the application.

4a) Of the above claim(s) *1-7 and 15-21* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *8-14 and 22-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-25* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/13/05;7/24/09*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of Group II (claims 8-14 & 22-25) in the reply filed on 6/04/09 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 1-7 & 15-21 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 6/04/09.

Claim Rejections - 35 U.S.C. § 112

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 8-14 & 22-25 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The specification describes on page 12, etc that "the substance[s] of the present invention that has the property of enhancing cGMP production through the NP receptor GC-A may be isolated in pure form from natural sources, chemically synthesized or recombinantly made", that

"those skilled in the art can obtain an appropriate substance in a known manner", and that *"[a]ny substance obtained* in any of these manners can be used as long as it is a substance capable of acting on the NP receptor GC-A to enhance cGMP production" [emphasis added]. In other words, except for the ANP or BNP peptides of SEQ ID NOs: 1-8, Applicants invite others to obtain the "substances" required to practice the instantly claimed method, which demonstrates that Applicants are not in possession of the genus of "substances" required to practice the currently claimed method of "treating" undefined Th-1-mediated immunes diseases (i.e., as it relates especially to claims 8, 12, 22 and 23). The issue becomes that without structurally defining what constitutes the claimed genus of "substances capable of acting on the NP receptor GC-A to enhance cGMP production", one of ordinary skill in the art would not know when they are in possession of the "substances" required to practice the currently claimed method. For example, one skilled in the art cannot reasonably visualize or predict what critical amino acid residues would structurally characterize the genus of "substances" that may constitute a formulation "for treating [unrelated or undefined] Th-1-mediated immune diseases", as claimed, since no Th-1 mediated immune disease is specially described within the instant specification that has been or reasonably could be treated with any compound/substance. To provide evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. Thus, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of use of the claimed genus of

substrances because one skilled in the art cannot structurally visualized any functional generic "substance" peptide, or amino acid sequences thereof, except possibly for the peptides of SEQ ID NOs: 1-8. In other words, because the specification fails to provide a representative number of species to show applicant is in possession of using the currently undefined genus of components required to practice the currently generic method, the written description requirements under 35 U.S.C. 112, first paragraph are not met. See MPEP 2163.

Accordingly, *Vas-Cath Inc. v. Mahurkar*, 19 USPQ2d 1111, 1117, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, *as of the filing date sought*, he or she was in possession *of the claimed invention*". "The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed* [emphasis added]".

3. Claims 8-14 & 22-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for decreasing graft rejection following transplantation comprising administering an effective amount of structurally and functionally characterized natriuretic peptides of SEQ ID NOs: 1-8, does not reasonably provide enablement for "treating" or preventing (as described on page 11 of the specification) known symptoms related to undefined "Th1-mediated immune diseases" with unknown etiology (i.e., as it relates to autoimmune diseases in general). The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification proposes a method of "Th1-mediated immune diseases" with undefined "substances capable of acting on the [undefined] natriuretic peptide receptor guanylyl cyclase A"

(i.e., as it relates to base claims 8 & 22). However, the mere correlation of cyclic guanosine monophosphate production with binding of ANP or BNP with its specific receptor provides no nexus for reasonably determining with how to treat any unrelated or undefined autoimmune disease state, each with their own etiology and consequences. In other words, there is no universal dysfunction in cyclic guanosine monophosphate metabolism that defines each and every autoimmune disease state, such as the laundry list recited in claim 10. Nor would one of ordinary skill in the art reasonably predict any expectation of success in treating undefined "Th-1-mediated immune disease" states with a single compound when different populations of cells and individuals are affected. The state f the art is well illustrated within the instant specification on pages 5 & 7 & 8, where it is stated that:

> "However, no clinically applicable pharmaceutical preparation has been developed that enables selective inhibition of Th1-mediated immunity and reduction of side effects".

It is noted that no specific Th-1 mediated immune disease condition involving dysfunction of natriuretic peptide is known in the art or disclosed in the instant specification, whose dysfunction is characterized by altered expression of ANP or BNP, at the time of filing Applicants' invention. Nor does the instant specification provide any guidance on how to reasonably "treat" and especially "prevent" any Th-1-mediated immune disease based solely on some putative "production of cyclic guanosine monophosphate; nor how to assay such *in vivo*.

Thus, because it is unknown what parameters are required to be assayed in order to determine when, or if, the instant invention is "effective" in treating any undefined "Th-1-mediated immune disease" condition, because the instant specification discloses no *in vivo* assays for determining when, or if, the Applicant's invention works *in vivo* or any "Th-1-mediated immune disease" is actually "treated", because it is not known nor disclosed how the

severity of symptoms (which are also not recited) are related to the efficacy of ANF or BNP, etc. and because it cannot be successfully extrapolated from the limited guidance provided within the instant specification whether the skilled artisan has successfully practiced Applicant's invention, it would require undue experimentation for the skilled artisan to know how to make and use the instant invention, as currently claimed, in light of the unpredictable state of the art in treating immune-related disease states.

Lastly, the name, "a substance capable of acting on the natriuretic peptide receptor guanylyl cyclase A to enhance production of cyclic guanosine monophosphate", or "an appropriate substance in a known manner by modification such as deletion, substitution, addition and/or insertion of amino acid residues in the sequence", as described on page 12 of the specification sets forth no structural characterization and little functional characteristics for knowing how to make and use the components required to practice the currently broad and ill-defined method of the instant invention. The specification fails to define what specific amino acids are critical for any "acting on [any structurally undefined] natriuretic peptide receptor guanylyl cyclase A" -related function, nor what amino acid residues distinguish the "substances" of the instant invention from any "substance" that does not work in the instantly claimed method. In contrast, the skilled artisan would reasonably expect that random mutations to any protein (i.e., as encompassed by the current claim language) would result in inactive "substance", and therefore a method that does not work. For example, Rudinger states on page 3 that "it is impossible to attach a unique significance to any residue in a sequence. A given amino acid will not by any means have the same significance in different peptide sequences, or even in different positions of the same sequence". Rudinger then states on page 6 that "the significance of

particular amino acid sequences for different aspects of biological activity cannot be predicted *a priori* but must be determined from case to case by painstaking experimental study". Therefore, the lack of guidance provided in the specification as to what minimal structural requirements are necessary for any "substance", or for even any ANP- or BNP-related peptide, to effect receptor binding or production of cyclic guanosine monophosphate would prevent the skilled artisan from determining whether any random modification or mutation to even the peptides of SEQ ID NO: 1 or 4, etc. could be made which retains the desired function of the instant invention, because any such random modification/ mutation manifested within an undefined "substance" required to practice the currently claimed method would be predicted to adversely affect the three-dimensional conformation of the "substance", without requiring undue experimentation to determine otherwise.

Conclusion

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Robert Hayes whose telephone number is (571) 272-0885. The examiner can normally be reached on Monday through Thursday from 9:00 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeff Stucker, can be reached on (571) 272-0911. The fax phone number for this Group is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-4797 (toll-free).

/Robert C. Hayes, Ph.D./
Primary Examiner, Art Unit 1649
August 10, 2009